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Mail Stop Appeal Brief - Patents
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Alexandria, VA 22313-1450

On June 3, 2003

TOWNSEND and TOWNSEND and CREW LLP

By: Dana Kane

9. Lawrence 7/18/03

PATENT

Attorney Docket No.: 015280-312100US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:

Seth R. Goldstein et al.

Application No.: 09/387,810

Filed: September 1, 1999

For: CONVEX GEOMETRY ADHESIVE FILM SYSTEM FOR LASER CAPTURE MICRODISSECTION

Examiner: Handy, Dwayne K.

Art Unit: 1743

APPEAL BRIEF

Mail Stop Appeal Brief - Patents
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Sir:

This is Appellants' Appeal Brief pursuant to 37 CFR §1.192.

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I. REAL PARTY IN INTEREST

The Government of the United States of America as represented by the Secretary of Health and Human Services is the real party in interest.

II. RELATED APPEALS AND INTERFERENCES

None

III. STATUS OF CLAIMS

Pursuant to an office action mailed December 3, 2002, claims 35 through 41 stand rejected as follows:

Claims 35 and 37-41 are rejected under 35 USC 102(e) as being anticipated by Liotta et al. (5,843,657).

Claim 36 is rejected under 35 USC 103(a) as being unpatentable over Liotta et al. (5,843,657) in view of Adams et al. (6,060,288).

IV. STATUS OF AMENDMENTS FILED SUBSEQUENT TO THE FINAL REJECTION

An Amendment Under 37 CFR 1.116 for Expedited Procedure Examining setting forth the argument appearing in this appeal was filed January 30, 2003. Pursuant to an Advisory Action mailed February 28, 2003, the arguments put forth were rejected.

V. SUMMARY OF INVENTION

Field of invention

The subject matter of this invention is directed to that field which has become known as "laser capture microdissection." In its original format, laser capture microdissection is described in Liotta et al. United States Patent 5,843,657 issued December 1, 1998. In that disclosure, a process of microdissection is disclosed. A sample having a portion for microdissection is contacted with a selectively activatable transfer surface. In its original state, the transfer surface is not adhesive to the sample. The sample is visualized for the portion of the sample it is desired to microdissect, this visualization typically being through the transfer surface (which preferably is transparent). Thereafter, the transfer surface is activated only at the portion of the transfer surface overlying the portion of the sample for microdissection. The activated portion of the transfer surface adheres to the sample portion. The nonactivated portion of the transfer surface does not adhere to the sample. When the transfer surface is removed, the sample portion adheres to the transfer surface portion and is removed. The microdissection occurs.

Understanding that this is the field in which this disclosure resides, the claimed elements of claim 35 can be summarized.

First, and as set forth in the preamble to claim 35, the disclosed apparatus is limited to laser capture microdissection.

Second, what we deal with here is a convex surface for placement to a sample. (Please note that the surface is not concave.)

Third, the convex surface is mounted to an extremity of the rod.

Fourth, a selectively activatable coating is placed over the convex surface. Like the transfer surface of Liotta et al. '657, the selectively activatable coating has nonadhesive properties. When activated this coating provides selected regions thereof with adhesive properties with respect to a sample. Non activated regions thereof remain with their non-adhesive properties. Using such a coating on a convex surface, laser capture microdissection can occur.

Claim 36 covers a convex surface which is spherical. In claim 37, the convex surface is faceted. In claim 38, the convex surface is cylindrical. In claim 39, the convex surface has the profile of a frustum. In claim 40, the rod and convex surface are transparent.

Claim 41 only adds the extraction of the dissected sample in a vial from the end of the probe.

VI. ISSUES

Is the rejection of claims 35 and 37-41 under 35 USC 102(e) as being anticipated by Liotta et al. (5,843,657) proper?

Is the rejection of claim 36 under 35 USC 103(a) as being unpatentable over Liotta et al. (5,843,657) in view of Adams et al. (6,060,288) proper?

VII. GROUPING OF CLAIMS

All claims 35-41 stand together or fall together.

VIII. ARGUMENT

Argument

Liotta et al. U.S. Patent 5,843,657 Disclosure Analyzed

This disclosure is directed to the process and apparatus for dissecting diseased tissue (usually cancer) in extraordinarily small samples down to and approaching the cellular level. In this disclosure, three discrete techniques of molecular dissection are discussed.

First Liotta et al. Embodiment

First, and referring to Fig. 3, conventional dissection of a sample (1) utilizing a cutting blade (10) and grasping arm (11) is disclosed.

This part of Liotta et al. '657 is not relevant to the rejection.

Second Liotta et al. Embodiment

Second, and referring to Figs. 2a to 2c, the use of a "sticky contact probe" is set forth for dissection of a sample (1) at a target sample zone B. In short, a contact probe (5) is provided. The end of the contact probe is provided with adhesive/extraction reagent (6). The contact probe (5) at the adhesive/extraction reagent (6) is contacted to the target sample zone B, the sample zone B adheres to the reagent (6) and is dissected and removed with the probe as the probe is removed.

There is an important limitation on the use of the "sticky contact probe." This limitation is provided at column 4, lines 35 through 41 of the Liotta et al. specification as follows:

> ... As can be readily understood from Fig. 2a, the surface area of the contact probe tip (and the adhesive-extraction reagent) needs to be about equal

to, and no greater than, the surface area of the zone to be extracted. Otherwise, excessive removal of adjacent tissue zones will occur.

This part of Liotta et al. ' 657 is relevant for the use of the probe. Since the probe does not have a "selectively activatable surface" it is sticky all of the time. When it contacts portions of the specimen it adheres.

The probe is flat at its end; it cannot be said to have a "convex" surface. Further, the size of the end of the probe is restricted as it is always sticky; it has to be less than "the surface area of the zone to be extracted." In other words, when the probe from this embodiment of Liotta et al. ' 657 is used as a reference, the limitation of the probe's use must follow. Finally, adhesive/extraction reagent is only placed at the flat end of the probe. It is not disclosed as being at any other part of the probe.

Third Liotta et al. Embodiment

Third, and referring to Figs. 8a to 8d, the first disclosure of laser capture microdissection is set forth. This material was added with the CIP that resulted in the cited reference.

A transfer surface (30) is utilized to extract targeted cellular material from cellular material (33) residing on support member (34). Initially in Fig 8a, transfer surface 30 having upper backing layer 31 and a lower activatable adhesive layer 32 overlies cellular material 33 residing on support member 34. Secondly in Fig 8b, contact occurs between the transfer surface 30 and the sample 33. Thirdly in Fig 8c, the transfer surface 30 is irradiated with a laser beam 36 overlying that part of the sample 33 where extraction is desired. Unlike the second Liotta embodiment where the probe is always sticky, this portion of the transfer surface (which is not a probe), only becomes sticky on "activation." Fourthly in Fig 8d, transfer layer 30 is lifted; an adhered portion of the sample 33 is dissected.

This part of Liotta et al. '657 is relevant for the use of the transfer surface. It has nothing to do with the use of a probe.

For the record, rejection of the claims was initially made in view of Liotta et al. (5,843,644). The examiner agreed with applicant that Liotta et al.' 644 did not disclose a selectively activated adhesive surface. The examiner "addressed this issue by replacing the original rejection with a new rejection based on the reference Liotta et al. (5,843,657) the relevant reference in this appeal." It was in this continuation in part from the original Liotta '644 that the following specification was added for the first time:

> According to a preferred embodiment, the present invention is directed to adhesive transfer methods which involved microscopic visualization and transfer of cellular material to a procurement or transfer surface.
>
> According to the general procedure, an adhesive surface is placed in contact with the surface of the cells or tissue and the adhesive force binds them the cellular material of interest to the adhesive surface. The adhesive surface which can be the tip of a tool or needle is used to procure the material and transfer it to a liquid analysis reaction mixture. Examples of adhesive surfaces include adhesive coatings on the tip of the tool, or the use of electrostatic forces between the tip and the surface of the cellular material.
>
> As described in detail below, the isolation and transfer methods of the present invention can involve a specialized continuous activatable adhesive layer or surface which is applied to the cellular material over an area larger than the area selected for microscopic procurement. The adhesive function of this subsection of the surface in contact with the areas selected for procurement is activated by electromagnetic or radiation means. According to a preferred embodiment, a laser or other electromagnetic radiation source is used to activate the adhesive forces between the cellular material and the activatable adhesive layer or surface. This allows for accurate generation of adhesive forces only in the precise microscopic areas selected area.... (Emphasis added) [Column 11, line 55 through column 12, line 13]

The reference then proceeds to described in detail Figs. 8A to 8D. A view of these figures indicates that the "activatable adhesive layer 32" is a continuous layer or surface placed over a "backing layer 31." No suggestion of application of the "specialized continuous

activatable adhesive layer or surface" material to either a small probe or an enlarged probe appears. Further, any probe is flat; no probe is rounded. It cannot be said that a convex surface is suggested.

35 USC 102(e) Rejection

For a rejection under 35 USC 102(e) to occur, the reference must show either an identical disclosure or that the combination is obvious. This is not the case when Liotta '657 is cited. The probe comes from the second Liotta embodiment above. The transfer surface comes from the third Liotta embodiment. Further, while importing the "elements" of the invention, the rejection does not support the actual use of the combination as used here. For example as taken from the second Liotta embodiment, the probe is used only once at its end, which end is flat. There is no suggestion the probe be rounded or provided with the convex surface for multiple usages. For further example as taken from the third Liotta embodiment, the transfer surface 30 is not shown attached to anything, certainly not a probe. This layer consists of a backing layer 31 and an activatable adhesive layer 32. There simply is no suggestion of combining the probe of the second Liotta embodiment with the transfer surface 30 of the third Liotta embodiment.

> "To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985).

35 USC 103 Rejection

Second, the rejection has cited Adams et al. (U.S. Patent 6,060,288). The rejection calls to appellants' attention cols. 16 lines 1 to 40 of Adams et al.' 288, portions of which are quoted here for convenience:

> ... Thus, the use of an optical fiber performs a three-fold function as the support for the amplification reaction, as a transmission means for the resultant signal and as a component of the detection system by transmitting this signal to the detector. [16: 7 to 12]

It can be seen from the above that dissection, let alone microdissection, is not a purpose of this disclosure. No mention of dissection is made.

But the disclosure continues further:

> One end of the optical fiber (referred to hereinafter as the distal end) is cleaved, polished, and then chemically modified to provide a surface having attachment sites for nucleic acid primers. A number of surface modification methods suitable for this purpose are known to those of skill in the art. For example, organosilane coating of glass and silica surfaces, ground polymerization on polymer surfaces, and/or high-voltage gas-plasmid discharges may be used to affect modification of glass, silica or polymer surfaces. The surface of the fiber may also be modified to have a convex or concave curvature to facilitate optical focusing. Following modification, oligonucleotides are then attached to the surface of the distal end of the fiber. This process usually involves several steps, which may include one or more of the following:
>
> a) Chemical treatment of the fiber surface to activated attachments sites for primer binding;
>
> b) Chemical treatment of the oligonucleotides to activate the groups which will interact with the fiber surface sites;
>
> c) Placing the modified fibers in contact with the oligonucleotides to allow immobilization reactions to occur; and,
>
> d) Treatment hand washing of the fiber surfaces to remove non-immobilized oligonucleotides, as well as any activation reagents or blocking groups that may interfere with the amplification reaction. (Emphasis added)

Reviewing the above quotation, the first thing to note is that the fiber and its distal end is "cleaved." "Cleave" is defined as:

cleave 1 [kleev] (past cleaved, cleft [kleft], clove [kl v], past participle cleaved, cleft, clo•ven, present participle cleav•ing, 3rd person present singular cleaves) transitive and intransitive verb

1. split: to split, or make something split, especially along a plane of natural weakness;

2. cut a path through: to make a way through something (literary) "We watched the bows of the tall ships cleave through the waves;" and

3. penetrate: to penetrate or pierce something deep or dense such as water or heavy undergrowth.

[Old English cl ofan . Ultimately from an Indo-European word that is also the ancestor of Greek gluphein "to carve" (source of English hieroglyphics).] (Microsoft Encarta Dictionary; Copyright 2002)

Applying this definition, the (distal) end of the optical fiber would look much like a cleaved branch having discrete separated "cleaved" portions splayed upwardly from the end of the optical fiber. This would give the appearance of a "broom," not of a rounded probe having a convex surface.

Second, chemical modification is undertaken. There is no indication that one portion of the distal fiber end is chemically treated while other portions of the distal fiber end are not chemically treated.

Then a statement is made about "the surface" of the fiber being given either a concave or convex surface to facilitate optical focusing." Insofar as this relates to the "cleaved distal end," it is not understood. How a cleaved end of the fiber can at the same time be provided with either a concave or a convex surface is not known. The only intelligible interpretation of the concave or convex surface is that it is somewhere on the fiber where light enters or exits the fiber.

Further, the reference - concerned with optics - suggests either concave or convex, interchangeably. In this disclosure, concave will not work; only convex is operative. Optics is obviously the only consideration; dissection is not considered.

One thing is clear. The reference teaches that oligonucleotides are attached at the cleaved distal end of the reference *en mass*. It would seem that the attachment of oligonucleotides to one portion of the distal end without attachment to other portions of the distal end is not at all contemplated. Further, dissection (especially microdissection) is never referred to anywhere in the reference.

If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). It is clear that the application of the cleaved structure of Adams et al. would change the landscape of the operation of the disclosed invention.

These statements are not directed at the "intended use" of the product. Instead, they point out that the claim limitations are not met by the reference insofar is it refers to "convex surface for placement to a sample" and "a selectively activated coating placed over the convex surface having nonadhesive properties which can be activated to provide selected regions thereof with adhesive properties when placed to a sample while non activated regions thereof remain with the non adhesive properties."

Finally, and principally because of the "cleaved" description of the distal end, it is not seen how over Adams et al. the claimed invention of claims 35 and 41 would be "obvious"

within the meaning of 35 USC 103, especially where these surfaces are mentioned with respect to optics and the optically reversible concepts of "concave or convex" are used.

It is submitted that when both Liotta '657 and Adams are fully understood, it is apparent that the invention is neither anticipated nor obvious over the references taken alone or in combination.

For the reasons given above, Appellants respectfully submit that the claims on appeal recite an invention that is patentably distinct over the cited prior art. Reversal of all rejections is respectfully requested.

Respectfully submitted,

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CLAIMS APPENDIX

35. (Once Amended) In an apparatus for laser laser capture microdissection, a contact surface comprising:

a convex surface for placement to a sample;

a rod with the convex surface mounted to an extremity of the rod; and,

a selectively activated coating placed over the convex surface having non-adhesive properties which can be activated to provide selected regions thereof with adhesive properties when placed to a sample while non activated regions thereof remain with the non-adhesive properties.

36. The apparatus for laser capture microdissection according to claim 35 wherein:

the convex surface is spherical.

37. The apparatus for laser capture microdissection according to claim 35 wherein:

the convex surface is faceted.

38. The apparatus for laser capture microdissection according to claim 35 wherein:

the convex surface is cylindrical.

39. The apparatus for laser capture microdissection according to claim 35 wherein:

the convex surface has the profile of a frustum.

40. The apparatus for laser capture microdissection according to claim 35 wherein:

the rod and convex surface are transparent.

41. (Once Amended) In an apparatus for laser capture microdissection, a contact surface and vial comprising:

a convex surface;

a selectively activated coating placed over the convex surface having non adhesive properties which can be activated to provide selected regions thereof with adhesive properties when placed to a sample while nonactivated regions thereof remain with the non-adhesive properties;

a vial having a dimension for permitting the convex surface to be placed into the vial; and,

a fluid in the vial for liberating at least part of the tissue sample adhered to the selectively activated convex surface.